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Evaluation of oxidative DNA cleavage of copper (II) complexes as chemotherapeutic agents

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Background and Aims: Transition metal complexes that are capable of cleaving DNA under physiological conditions are of interest in the development of metal-based anticancer agents. DNA cleavage may take place via hydrolytic or oxidative pathways. Previous studies showed that copper complexes could bind to DNA and show cytotoxicity activity. Herein, we decided to evaluate the nuclease activity of two copper complexes (1, 2) in order to find new compounds in chemotherapy.
Methods: The DNA cleavage activity of two complexes [1: [Cu(tpy)(dppz)](PF6)2] and [2: [Cu(tptz)2] (PF6) 2•CH3CN] was studied using supecoiled pEGFP-N1 by 0.7% agarose gel electrophoresis after incubated at 37°C for 3h. The gels were stained and viewed under UV light. The percentage of cleavage of supercoiled DNA was quantified by measuring of the bands using Image J software. Cell cytotoxicity was determined using MTT assay on MCF-7 cell line.
Results: Copper (II) complexes (1, 2) exhibit a remarkable DNA cleavage activity. In order to obtain information about the mechanism of these complexes (1, 2), we investigated the DNA cleavage of the complexes (1, 2) by gel electrophoresis in the presence of various radical scavengers such as NaN3 (singlet oxygen quenchers), DMSO (hydroxyl radical scavenger) and SOD (superoxide dismutase, superoxide scavenger), suggesting the involvement of active oxygen species for the DNA scission. Investigation of the cleavage activity of the complexes (1, 2) in the presence of activator (H2O2) also exhibited pronounced nuclease activity which confirmed our previous data. Both complexes indicated cytotoxic effect on MCF-7cell line, with IC50 values of 4.57 µM (3.62–5.77) and 1.4 µM (0.9-2.1), respectively
Conclusions: Our results found that these complexes (1, 2) may have potential to act as effective metal-based anticancer drugs.

Keywords: DNA Cleavage; MCF-7; MTT; COMPLEX